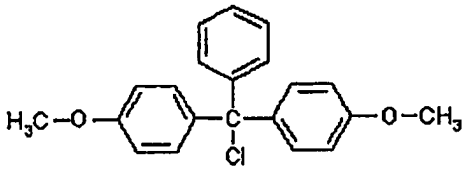
EXHIBIT A

GL Biochem (Shanghai) Ltd
吉尔生化（上海）有限公司

Product Specification

Name: **DMT-Cl**
Category: N-Protecting Reagents



Product Data Sheet

Product Name	DMT-Cl; 4,4'-Dimethoxytrityl chloride; 4,4'-Dimethoxytriphenylmethyl chloride
CAS No.	40615-36-9
Molecular Formula	$C_{21}H_{19}ClO_2$
Molecular Weight	338.8
Appearance	Light pink color powder
Purity (HPLC)	98% min.
Melting Point	120-125 °C (dec.)
TLC Analysis	One spot
300 MHz ^{1}H NMR Spectrum ($CDCl_3$)	Consistent
Loss on Drying	< 0.5%
Solubility Test (In Pyridine)	Clear solution with 1g/10ml
Solvent of Recrystallization	Benzene, Hexanes
Use Test	Passed

EXHIBIT B

PROTECTIVE GROUPS IN ORGANIC SYNTHESIS

Second Edition

THEODORA W. GREENE
The Rowland Institute for Science, Inc.

and

PETER G. M. WUTS
The Upjohn Company

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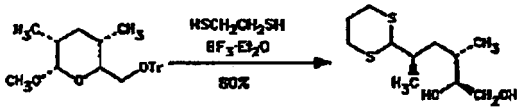
PREFACE TO THE SECOND EDITION

Since publication of the first edition of this book in 1981, many new protective groups and many new methods of introduction or removal of known protective groups have been developed: 206 new groups and approximately 1500 new references have been added. Most of the information from the first edition has been retained. To conserve space, generic structures used to describe Formation/Cleavage reactions have been replaced by a single line of conditions, sometimes with explanatory comments, especially regarding selectivity. Some of the new information has been obtained from Online Searches of Chemical Abstracts, which have limitations. For example, Chemical Abstracts indexes a review article about protective groups only if that word appears in the title of the article. References are complete through 1989. Some references, from more widely circulating journals, are included for 1990.

Two new sections on the protection for indoles, imidazoles, and pyrroles, and protection for the amide —NH are included. They are separated from the regular amines because their chemical properties are sufficiently different to affect the chemistry of protection and deprotection. The Reactivity Charts in Chapter 8 are identical to those in the first edition. The chart number appears beside the name of each protective group when it is first discussed.

A number of people must be thanked for their contributions and help in completing this project. I am grateful to Gordon Bundy, who loaned me this card file, which provided many references that the computer failed to find, and to Bob Williams, Spencer Knapp, and Tohru Fukuyama for many references on amine and amide protection. I thank Theo Greene who checked and rechecked the manuscript for spelling and consistency and for the herculean task of checking all the references to make sure my 3s and 8s and 7s and 9s were not interchanged, all without

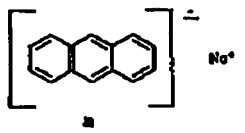
12. Et_2AlCl, CH_2Cl_2, 3 min, 70–85% yield.[19] This method was used to remove the trityl group from various protected deoxyribonucleotides. The TBDPS group is stable to these conditions.
13. TsOH, MeOH, 25°, 5 h.[20]
14. $BF_3 \cdot Et_2O$, $HSCH_2CH_2SH$, 80% yield.[21]



15. Na, NH_3.[22] Benzyl groups are also removed under these conditions.
16. $ZnBr_2$, MeOH, 100% yield.[23]

57. α-Naphthyldiphenylmethyl Ether: RO–$C(Ph)_2$–α-$C_{10}H_7$ (Chart 1)

The α-naphthyldiphenylmethyl ether was prepared to protect, selectively, the 5′-OH group in nucleosides. It is prepared from α-naphthyldiphenylmethyl chloride in pyridine (65% yield), and cleaved selectively in the presence of a *p*-methoxyphenyldiphenylmethyl ether with sodium anthracenide, a (THF, 97% yield). The *p*-methoxyphenyldiphenylmethyl ether can be cleaved with acid in the presence of this group.[24]



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58. *p*-Methoxyphenyldiphenylmethyl Ether (MMTrOR): *p*-$MeOC_6H_4(Ph)_2C$–OR (Chart 1)

59. Di(*p*-methoxyphenyl)phenylmethyl Ether (DMTrOR): $(p\text{-}MeOC_6H_4)_2PhC$–OR

60. Tri(*p*-methoxyphenyl)methyl Ether (TMTrOR): $(p\text{-}MeOC_6H_4)_3C$–OR

These were originally prepared by Khorana[25] as selective protective groups for the 5′-OH of nucleosides and nucleotides. They were designed to be more acid-labile than the trityl group because depurination is often a problem in the acid-catalyzed removal of the trityl group. Introduction of *p*-methoxy groups increases the rate of hydrolysis by about one order of magnitude for each *p*-methoxy substituent. For 5′-protected uridine derivatives in 80% AcOH, 20°, the time for hydrolysis was

as follows:

$(p\text{-}MeOC_6H_4)_n(Ph)_mCOR$

$n = 0, m = 3$, 48 h
$n = 1, m = 2$, 2 h
$n = 2, m = 1$, 15 min
$n = 3, m = 0$, 1 min

The trimethoxy derivative is too labile for most applications, but the mono and di-derivatives have been used extensively in the preparation of oligonucleotides and oligonucleosides. The monomethoxy derivative has been used for the selective protection of a primary allylic alcohol over a secondary allylic alcohol (MMTr, Pyr, −10°).[26]

Cleavage

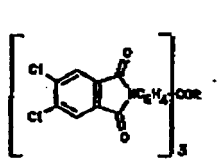
In practice the various trityl derivatives are cleaved with acid, but the monomethoxy derivative can be cleaved with sodium naphthalenide in HMPA (90% yield).[27] It is not cleaved by sodium anthracenide, used to cleave α-naphthyldiphenylmethyl ethers.[24]

A solution of 3% CCl_3CO_2H in 95:5 CH_3NO_2/MeOH is recommended for removal of the DMTr group from the 5′-OH of deoxyribonucleotides because of reduced levels of depurination compared to Cl_3CO_2H/CH_2Cl_2, $PhSO_3H$/MeOH/CH_2Cl_2, and $ZnBr_2/CH_3NO_2$.[28]

61. 4-(4′-Bromophenacyloxyphenyl)diphenylmethyl Ether: *p*-($p\text{-}BrC_6H_4C(O)CH_2O$)$C_6H_4(Ph)_2C$–OR

This group was developed for protection of the 5′-OH group in nucleosides. The derivative is prepared from the corresponding triarylmethyl chloride, and is cleaved by reductive cleavage (Zn/AcOH) of the phenacyl ether to the *p*-hydroxyphenyldiphenylmethyl ether followed by acidic hydrolysis with formic acid.[29]

62. 4,4′,4″-Tris(4,5-dichlorophthalimidophenyl)methyl Ether (CPTr–OR):



The CPTr group was developed for the protection of the 5′-OH of ribonucleosides. It is introduced with CPTrBr/$AgNO_3$/DMF (15 min) in 80–96% yield and can be removed by ammonia followed by 0.01 *M* HCl or 80% AcOH.[30] It can also be removed with hydrazine and acetic acid.[31]